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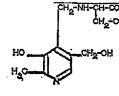
(19)

(54) PYRIDOXYL-*l*-ASPARTIC ACID SALT

(71) We, SOCIETE D'ETUDES DE PRODUITS CHIMIQUES, a company organised and existing under the laws of France, of 16 rue Kleber 92130 Issy-Less-Moulineaux, France, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to mono-potassium-pyridoxyl aspartate, to a method for its manufacture and to therapeutic compositions containing it.

The mono-potassium-pyridoxyl-*l*-aspartate of the invention has the formula I;



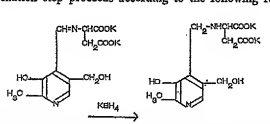
I

This compound is a white powder melting at 240°C to 245°C, soluble in water, insoluble in chloroform and in ethanol. The pH of an aqueous solution containing 5% of this product is 5.7.

The invention also provides a method for preparing the above compound, comprising reacting pyridoxal, preferably in solution in methanol, with dipotassium-*l*-aspartate; hydrogenating the resulting Schiff's base with potassium borohydride KBH, and converting the resulting di-potassium salt into the mono-potassium salt by an appropriate addition of a mineral acid.

By using potassium borohydride as the hydrogenating agent it is possible to obtain a yield of about 66%.

The hydrogenation step proceeds according to the following reaction scheme:



Pharmacological experiments have shown satisfactory cardiac analeptic action at doses from 20 mg/kg. I.V. on anaesthetized dogs and an anti-fibrillary action at doses from 100 mg/kg I.P., on mice by the technique of Lawson. The invention accordingly provides a therapeutic composition comprising the salt according to the invention in admixture with an inert diluent or carrier, suitably in unit dosage form.

The following Example illustrates the invention.

Example

In a 10 litre reactor there were poured 5 litres of dried methanol and 112 g of potassium hydroxide. The reactor was heated to 30°C and there were added 133.1 g of aspartic acid whilst stirring. 15 minutes later there were added, whilst stirring,

167.2 g of pyridoxal and stirring was maintained for one hour at room temperature to obtain a yellow solution. The reaction mixture was then heated to 30°C, there were slowly added 13.5 g of potassium borohydride, whilst stirring, and the reaction mixture was maintained for 2 hours at room temperature. The colourless solution thus obtained was cooled in an ice bath and there were added 30 g of acetic acid dissolved in a sufficient amount of water to give 240 ml of solution. The water added served to effect the degradation of the non-reacted potassium borohydride. Stirring was maintained for one hour and there were added 440 g of acetic acid diluted in methanol to give 1 litre of solution. The mixture was stirred for 2 days.

There was obtained a white precipitate which was separated, washed with methanol, rinsed with diethyl ether and then dried.

Yield: 215 g (66%).

WHAT WE CLAIM IS:—

1. Mono-potassium-pyridoxyl-*l*-aspartate of the formula I herein.

2. A process for the preparation of mono-potassium-pyridoxyl-*l*-aspartate consisting in reacting pyridoxal with di-potassium-*l*-aspartate, hydrogenating the resulting base with potassium borohydride and converting the resulting di-potassium salt into the corresponding mono-potassium salt by an appropriate addition of mineral acid.

3. A process according to claim 2, wherein the pyridoxal is reacted with the di-potassium-*l*-aspartate in solution in methanol.

4. A process for the preparation of mono-potassium-pyridoxy-*l*-aspartate substantially as described in the Example herein.

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